

Table of Contents

| | |
|--|-----------|
| Acknowledgements | 4 |
| Abstract | 6 |
| Resumé (Dansk) | 8 |
| List of papers included in the thesis | 10 |
| Aim of the studies | 11 |
| 1. Introduction | 13 |
| 2. Insulin-stimulated glucose uptake in skeletal muscle | 15 |
| 2.1. Delivery | 16 |
| 2.2. Transport | 18 |
| 2.2.1. Glucose transporters | 18 |
| 2.2.2. Insulin signaling to GLUT4 translocation | 18 |
| 2.3. Metabolism..... | 22 |
| 2.4. Is there a rate limiting step for insulin-stimulated glucose uptake? | 23 |
| 3. Acute exercise-induced insulin sensitivity for glucose uptake | 25 |
| 3.1. Adaptations important for glucose delivery | 26 |
| 3.2. Adaptations important for glucose transport | 27 |
| 3.2.1. GLUT4..... | 28 |
| 3.2.2. Insulin signaling in response to exercise | 29 |
| 3.2.3. Potential role for AMPK-TBC1D4 in the insulin-sensitizing effect of a single bout of exercise | 30 |
| 3.2.4. Other candidates important for glucose transport..... | 33 |
| 3.3. Adaptations important for intracellular metabolism of glucose | 34 |
| 3.3.1. Hexokinase | 34 |
| 3.3.2. Glycogen..... | 35 |
| 3.3.3. Glycogen synthase | 37 |
| 3.4. Exercise training and insulin sensitivity..... | 38 |
| 3.4.1. The insulin-sensitizing effect of a single bout of exercise and the effect of training status | 39 |
| 3.4.2. AMPK expression and activation in the trained muscle..... | 41 |
| 3.5. Important premises for the measurements of insulin sensitivity | 44 |
| 4. Acute exercise-induced “insulin resistance” | 45 |
| 4.1. Insulin action in the non-exercised tissue | 46 |
| 4.2. Lipid-induced insulin resistance..... | 48 |
| 4.2.1. Intracellular metabolism – the glucose-fatty acid cycle | 49 |
| 4.2.2. Impaired proximal insulin signaling..... | 52 |
| 4.2.3. Downstream signaling of Akt..... | 54 |
| 4.2.4. Non-oxidative glucose metabolism | 56 |
| 4.3. The amount of active vs. inactive muscle mass | 56 |
| 4.4. The one-legged knee-extensor model | 59 |
| 5. Muscle fiber types and insulin sensitivity for glucose uptake | 61 |
| 5.1. Morphological and metabolic differences between fiber types | 61 |
| 5.2. Fiber types and insulin sensitivity for glucose uptake | 63 |

| | |
|--|-----------|
| 5.3. Effect of training | 67 |
| 5.4. Acute exercised-induced insulin sensitivity in a fiber type-specific manner | 68 |
| 5.5. Methodological considerations of fiber type-specific measurements and the use of proteomics | 70 |
| 5.5.1. Fiber type-specific measurements | 70 |
| 5.5.2. Methodological considerations regarding the proteomic analysis | 72 |
| 6. Conclusion and future directions | 75 |
| 7. References | 77 |
| 8. Appendix | 93 |